

Application No.: Not Yet Assigned

Docket No.: 0933-0232PUS1

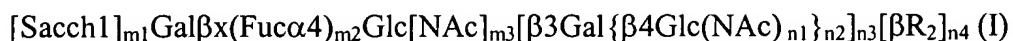
DT01 Rec'd PCT/EP 17 DEC 2004

AMENDMENTS TO THE CLAIMS

Claims 1-75 have been cancelled.

76. (New) A therapeutical composition containing purified fraction(s) of at least two compounds being or containing a pathogen inhibiting oligosaccharide sequence selected from the pathogen receptors

as defined in the formula



wherein x is linkage position 3 or 4, Sacch1 is GlcNAc $\beta$ 3, Gal $\alpha$ 3, GalNAc $\beta$ 4, Gal $\alpha$ 4, or Neu5X $\alpha$ 3/6, in which X is independently either Ac or Gc;

n1, n2, n3, n4, m1, m2, and m3 are independently integers 0 or 1

with the provisions that m2 may be 1 only when x is 3, m1 is 0, and m3 is 1;

m3 may be 0 only when Sacch1 is Neu5X $\alpha$ 3, Neu5X $\alpha$ 6, Gal $\alpha$ 3, GalNAc $\beta$ 4 or Gal $\alpha$ 4;

when n4 is 1, then m3 is 0 and n3 is 0, and

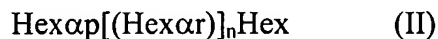
when n4 is 0, then m1 is 1, m2 is 1, or n3 is 1;

R<sub>2</sub> is a ceramide comprising a hydroxyl fatty acid or an analog of a ceramide comprising a hydroxyl fatty acid;

Sacch1 is Gal $\alpha$ 3 or GalNAc $\beta$ 4 with the provision that when the composition contains at least two receptors according to formula (I), these have at least one different variable selected from the group consisting of Sacch1, x, m2, and n4 with the provision that two sialic acid receptors or two neolacto receptors cannot be selected;

with the provision that when Sacch1 is Gal $\alpha$ 4, Neu5X $\alpha$ 3, Neu5X $\alpha$ 6, or GalNAc $\beta$ 4, the oligosaccharide sequence according to the formula I may be a partial oligosaccharide sequence Gal $\alpha$ 4Gal, Neu5X $\alpha$ 3Gal, Neu5X $\alpha$ 6Gal, or GalNAc $\beta$ 4Gal; and

with the provision that when the composition contains only one receptor according to formula (I) then it is together with at least one alpha-hexose receptor as defined in the formula



wherein Hex is Gal or Man, n is independently 0 or 1, p and r are linkage position 3 or 6 between Man residues, with the provision that when Hex is Man, then p is 3 and then r is 6, and when p is 6, then r is 3, and when Hex is Gal, then p is 4 and n is 0, with the provision that when Hex is Gal, it is not with Gal $\alpha$ 4Gal-receptor according to the formula I.

77. (New) The composition according to claim 76, wherein the terminal activating sequence is Gal $\alpha$ 4 and the composition comprises the partial epitope Gal $\alpha$ 4Gal and a Mannose receptor comprising the oligosaccharide sequence



wherein n is 0 or 1.

78. (New) The composition according to claim 76 containing purified fraction(s) of at least two compounds being or containing a pathogen inhibiting oligosaccharide sequence selected from the pathogen receptors as defined by the formula

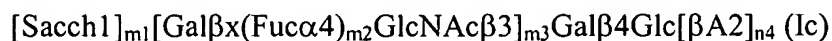


wherein  $m3$  and  $n4$  are independently integers 0 or 1;

wherein the natural type non-reducing end activator sequence A1 is selected from the group consisting of GalNAc $\beta$ 4, Gal $\alpha$ 4, Neu5X $\alpha$ 3, Neu5X $\alpha$ 6, GalNAc $\beta$ 3Gal $\alpha$ 4, Gal $\beta$ 3GalNAc $\beta$ 4, Gal $\beta$ 4GlcNAc $\beta$ 3, GlcNAc $\beta$ 3Gal $\beta$ 4GlcNAc, Gal $\beta$ 3GlcNAc $\beta$ 3, Neu5X $\alpha$ 3Gal $\beta$ 4GlcNAc $\beta$ 3, Neu5X $\alpha$ 6Gal $\beta$ 4GlcNAc $\beta$ 3, and Gal $\beta$ 3(Fuc $\alpha$ 3)GlcNAc $\beta$ 3; and wherein X is independently either Ac or Gc, and A2 is a ceramide comprising a hydroxyl fatty acid or an analog of a ceramide comprising a hydroxyl fatty acid.

79. (New) The composition according to claim 78, wherein A1 is selected from the group consisting of Gal $\alpha$ 4, Neu5X $\alpha$ 3, Neu5X $\alpha$ 6, Gal $\beta$ 4GlcNAc $\beta$ 3 or Gal $\beta$ 3GlcNAc $\beta$ 3.

80. (New) The composition according to claim 76 containing purified fraction(s) of at least two compounds being or containing a pathogen inhibiting oligosaccharide sequence selected from the pathogen receptors as defined by the formula



wherein x is linkage position 3 or 4, Sacch1 is GlcNAc $\beta$ 3, Gal $\alpha$ 3, GalNAc $\beta$ 4, Gal $\alpha$ 4, or Neu5X $\alpha$ 3/6, in which

X is independently either Ac or Gc;

n4, m1, m2, and m3 are independently integers 0 or 1,

with the provisions that m2 is 1 only when x is 3,

when Sacch1 is GlcNAc $\beta$ 3, then m3 is 1 and x is 4, and

m3 may be 0 only when m1 is 1 or n4 is 1,

when n4 is 0, then m1 is 1 or m3 is 1;

A2 is a ceramide comprising a hydroxyl fatty acid or an analog of a ceramide comprising a hydroxyl fatty acid, and

with the provision that at least two receptors are selected so that these have at least one different variable selected from the group Sacch1, x, m2, n4, preferably with the provision that not two sialic acid receptors are selected.

81. (New) The composition according to claim 76 containing purified fraction(s) of at least two compounds being or containing a pathogen inhibiting oligosaccharide sequence selected from the pathogen receptors as defined by the formula



wherein x is linkage position 3 or 4, Sacch1 is Gal $\alpha$ 4, Neu5X $\alpha$ 3 or Neu5X $\alpha$ 6, wherein X is independently either Ac or Gc;

m1, and m3 are independently integers 0 or 1,

with the provision that either m1 is 1 or m3 is 1,  
with the provision that at least two receptors are selected so that these have at least one different variable Sacch1 or x, preferably with the provision that not two sialic acid receptors are selected.

82. (New) The composition according to claim 81, wherein the oligosaccharide sequences are selected from the group consisting of Gal $\alpha$ 4Gal $\beta$ 4Glc, NeuNAc $\alpha$ 3Gal $\beta$ 4Glc, NeuNAc $\alpha$ 6Gal $\beta$ 4Glc, NeuNAc $\alpha$ 3Gal $\beta$ 4GlcNAc, NeuNAc $\alpha$ 6Gal $\beta$ 4GlcNAc, Gal $\beta$ 4GlcNAc $\beta$ 3Gal $\beta$ 4Glc and Gal $\beta$ 3GlcNAc $\beta$ 3Gal $\beta$ 4Glc.

83. (New) The composition according to claim 76, wherein at least one sialylated oligosaccharide, preferably a bovine milk fraction comprising sialylated oligosaccharides, such as NeuNAc $\alpha$ 3Gal $\beta$ 4Glc, NeuNAc $\alpha$ 6Gal $\beta$ 4Glc or NeuNAc $\alpha$ 6Gal $\beta$ 4GlcNAc, is used together with at least one neutral oligosaccharide, preferably Gal $\alpha$ 4Gal $\beta$ 4Glc, Gal $\alpha$ 4Gal, Gal $\beta$ 4GlcNAc $\beta$ 3Gal $\beta$ 4Glc (LNnT) or Gal $\beta$ 3GlcNAc $\beta$ 3Gal $\beta$ 4Glc (LNT).

84. (New) The composition according to claim 81, wherein said pathogen inhibiting oligosaccharides comprise a mixture of two different types of oligosaccharides selected from the group consisting of globo-oligosaccharides, Neolacto-oligosaccharides, and sialyl-oligosaccharides, preferably Gal $\beta$ 4GlcNAc $\beta$ 3Gal $\beta$ 4Glc, Gal $\alpha$ 4Gal $\beta$ 4Glc, and/or sialyllactoses.

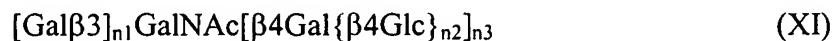
85. (New) The composition according to claim 76 comprising a purified fraction(s) of at least two compounds being or containing a pathogen inhibiting oligosaccharide sequence selected from at least two of the following groups of pathogen receptors:

a) lactosylceramide receptors as defined in the formula



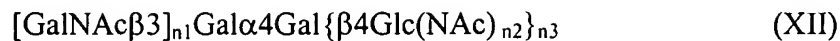
wherein x is linkage position 3 or 4,  $R_2$  is a ceramide comprising a hydroxyl fatty acid or an analog of a ceramide comprising a hydroxyl fatty acid, and  $R_1$  is  $\text{Gal}\alpha$ ,  $\text{Gal}\beta$ ,  $\text{GalNAc}\beta$ ,  $\text{GlcNAc}\beta$  or a longer oligosaccharide comprising  $\text{Gal}\alpha$ ,  $\text{Gal}\beta$ ,  $\text{GalNAc}\beta$  or  $\text{GlcNAc}\beta$  at the reducing end or  $\text{Neu5X}\alpha$ , wherein X is Ac or Gc, with the proviso that when  $R_1$  is  $\text{GlcNAc}\beta$  or  $\text{Neu5X}\alpha$  then x is 3;

b) ganglio-receptors as defined in the formula



wherein  $n1$ ,  $n2$  and  $n3$  are independently integers 0 or 1, with the proviso that either  $n1$  or  $n3$  is 1, and with the proviso that no sialic acids are linked to the oligosaccharide sequence;

c)  $\text{Gal}\alpha 4\text{Gal}$ -receptors as defined in the formula



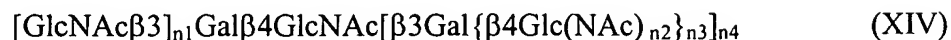
wherein  $n1$ ,  $n2$ , and  $n3$  are independently integers 0 or 1, and the GalNAc-residue is optionally further substituted by other monosaccharide residues;

d) lacto-receptors as defined in the formula



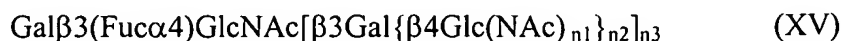
wherein  $n1$ ,  $n2$ , and  $n3$  are independently integers 0 or 1;

e) neolacto-receptors as defined in the formula



wherein  $n1$ ,  $n2$ ,  $n3$  and  $n4$  are independently integers 0 or 1, when  $n1$  is 1, the non-reducing terminal GlcNAc can be further substituted by a monosaccharide residue or an oligosaccharide;

f) fucosyl-receptors as defined in the formula



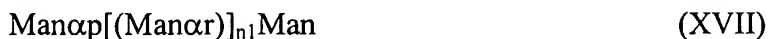
wherein  $n_1$ ,  $n_2$ , and  $n_3$  are independently integers 0 or 1;

g) sialic acid-receptors as defined in the formula



wherein independently X is either Ac or Gc meaning that the sialic acid is either Neu5Ac or Neu5Gc,  $n_1$  and  $n_2$  are either 0 or 1, p is linkage position 3 or 6, r and s are linkage positions 3 or 4 with the proviso that when r is 3 then s is 4 and when r is 4 then s is 3;

h) mannose receptors as defined in the formula



wherein n is independently 0 or 1, p and r are linkage position 3 or 6 between the Man residues, with the proviso that when p is 3 then r is 6, and when p is 6 then r is 3.

86. (New) The composition according to claim 85, wherein the pathogen receptor of group a) is selected from the group of receptor oligosaccharide sequences consisting of:



lactosylceramide, lactosylceramide comprising hydroxyl fatty acids, lactosylceramide with modified carbon 3 of a galactose residue and isoglobotriaocylceramide

87. (New) The composition according to claim 85, wherein the pathogen receptor of group g) is selected from the group of receptor oligosaccharide sequences consisting of:

oligosaccharides with Neu5X $\alpha$ 3Gal $\beta$ 3(Fuc $\alpha$ 4)GlcNAc, Neu5X $\alpha$ 3Gal $\beta$ 4(Fuc $\alpha$ 3)GlcNAc, Neu5X $\alpha$ 3Gal $\beta$ 4(Fuc $\alpha$ 3)Glc, Neu5X $\alpha$ 3Gal $\beta$ 3GlcNAc, Neu5X $\alpha$ 3Gal $\beta$ 4GlcNAc, Neu5X $\alpha$ 3Gal $\beta$ 4Glc, Neu5X $\alpha$ 6Gal $\beta$ 4GlcNAc or Neu5X $\alpha$ 6Gal $\beta$ 4Glc structures

88. (New) The composition according to claim 76, wherein at least one of said compounds is in monovalent form optionally being a glycosylamine or a glycosylamide or a methyl glycoside or a glycoside including other N-glycosides, C-glycosides or S-glycosides.

89. (New) The composition according to claim 76, wherein at least one of said compounds is linked to a polyvalent carrier.

90. (New) The composition according to claim 89, wherein said polyvalent carrier is a carbohydrate carrier or a particle carrier or a soluble carbohydrate carrier, or a particle carrier or a bacterial polysaccharide or part of bacterial polysaccharide also comprising the receptor

oligosaccharide sequence, or a carbohydrate particle, a synthetic polymer particle or a cell, or an antigenic or immunostimulating carbohydrate conjugate.

91. (New) The composition according to claim 76 further comprising one or several oligosaccharide sequences selected from the group of:

oligosaccharides comprising sequences  $\text{Fuc}\alpha 2\text{Gal}$ ,  $\text{Fuc}\alpha 3\text{GlcNAc}$ ,  $\text{Fuc}\alpha 3\text{Glc}$ ,  $\text{NeuNAc}\alpha 8\text{NeuNAc}$ ,  $\text{Fuc}\alpha 2\text{Gal}\beta 3/4\text{GlcNAc}$ ,  $\text{Fuc}\alpha 2\text{Gal}\beta 4\text{Glc}$ ,  $\text{Fuc}\alpha 2\text{Gal}\beta 4(\text{Fuc}\alpha 3)\text{Glc}$ ,  $\text{Gal}\beta 4(\text{Fuc}\alpha 3)\text{GlcNAc}$ ,  $\text{Fuc}\alpha 2\text{Gal}\beta 3/4(\text{Fuc}\alpha 4/3)\text{GlcNAc}$  and ganglioseries ganglioside oligosaccharide sequences.

92. (New) A method of treatment for a bacterial infection, wherein a pharmaceutically or therapeutically or prophylactically effective amount of the composition of claim 76 is administered to a subject in need of such treatment.

93. (New) The method according to claim 92, wherein said bacterial infection is a gastrointestinal infection.

94. (New) The method according to claim 92, wherein said gastrointestinal infection causes diarrhea or traveller's diarrhea, children's diarrheas, persistent diarrhea, watery diarrhea, hemorrhagic colitis or haemolytic uremic syndrome.

95. (New) The method according to claim 92, wherein said infection is caused by EPEC (enteropathogenic *Escherichia coli*), ETEC (enterotoxigenic *Escherichia coli*), EHEC (enterohemorrhagic *Escherichia coli*), EIEC (enteroinvasive *Escherichia coli*) or EAEC (enteroaggregative *Escherichia coli*).

96. (New) The method according to claim 92, wherein said infection is caused by *Vibrio* species including *Vibrio cholerae*, *Campylobacter* species including *Campylobacter jejuni*, intestinal eukariotic parasites including the *Entamoeba* species, *Salmonella* including *Salmonella typhimurium*, *Shigella* species, *Aeromonas* species, zoonotic *Helicobacter* species, *Listeria* species or rotavirus or the cause of infection is not diagnosed.

97. (New) The method according to claim 91, wherein said subject is a human patient or an animal patient.

98. (New) A method of improving food safety comprising a step of coating a food product with a composition according to claim 76.

99. (New) A nutritional composition or a nutritional additive or infant formula comprising a purified fraction(s) of at least of two compounds as defined in claim 76 for prophylaxis or treatment of gastrointestinal infection optionally further comprising a probiotic microorganism or a prebiotic substance.

100. (New) A product for inhibition of pathogens, especially diarrhea causing *E. coli*, *ex vivo* comprising a purified fraction(s) of at least of two compounds as defined in claim 76, wherein said product is selected from the group consisting of: a mouth hygiene product, a food coating product, a food preservative, or a topical, washing, or cosmetic product.

101. (New) A method of analysis or diagnostics comprising a step of contacting a putative pathogenic or probiotic microbe with at least three pathogen receptors as defined in claim 76.

102. (New) A method of analysis or diagnostics comprising a step of contacting a putative pathogenic or probiotic microbe with a receptor selected from the group consisting of:

lacto-receptors, neolacto-receptors, fucosyl-receptors, mannose receptors or sialic acid receptors

for analysis or diagnosis of pathogen or probiotic binding,

wherein the said receptors are

i) protein linked receptors and

ii) comprising a terminal non-reducing end oligosaccharide sequence present in the epithelium of human intestine, human stomach or human larynx.

103. (New) A method for a search or design of bacteria binding oligosaccharide substances comprising a step of modelling the binding properties of the oligosaccharide receptors as defined in claim 76.

104. (New) A diarrheagenic *E. coli* inhibiting substance according to the formula



wherein PO is an oligomeric or polymeric carrier structure, OS is an oligosaccharide sequence according to the invention, n is an integer  $\geq 1$  indicating the number of oligosaccharide groups covalently attached to the carrier PO, S is a spacer group, p, q and r are each 0 or 1, whereby at least one of p and r is different from 0, y and z are linking groups, at least one of y and z being an O-hydroxylamine residue  $-\text{O}-\text{NH}-$  or  $-\text{O}-\text{N}=\text{}$ , with the nitrogen atom being linked to the OS and/or PO structure, respectively, and the other y and z, if present, is a chemoselective ligation group.